

Two fifteen-year olds, let's call them Rick and Jim, decide they are curious about alcohol, having never tried it. They convince an older friend to buy them a case of beer and one night, while parents are out of town, they settle down for a night of drinking and gaming. Good friends, they decide that they will drink each beer in tandem, so that neither "gets ahead." By the end of the night, they have consumed the case, and are perfectly matched for their alcohol drinking history: 12 beers each. Five years later, Rick is well on his way to becoming an alcoholic, drinking daily and bingeing every weekend. Jim, still under-age, has relatively little interest in alcohol, and spends his weekends fishing and studying.

Many of us have met kids like Rick and Jim, and watched them veer down different roads as they grow up. So why do some of us develop into problem drinkers, while others do not? This question has long interested lay people and scientists alike, and answers are beginning to emerge from a wide range of fields including behavioral genetics, neuroscience, and psychology. One way that people have asked the question is about whether genes or environment affected the way Rick and Jim responded to alcohol the first time they drank it. For example, did Rick enjoy alcohol more? Did he get more or less drunk than Jim, or have less of a hangover? The evidence on this issue is clear: there are genetic differences among us in how we feel when we drink alcohol. The largest single difference (that is, a difference in just one important gene) was discovered right here in Indiana by researchers at the Alcohol Research Center. They found that some of us have livers that make us feel ill when we drink because we have difficulty metabolizing the poisons created by breaking down alcohol. The minority who have these livers (and they are mostly found among those of East Asian or Ashkenazi Jewish descent) have relatively little chance of becoming an alcoholic.

What about the rest of us, who have livers that do not make us feel ill when we drink? Increasingly, we are finding that differences among us may actually predate our troubles with alcohol, and perhaps even our first drink. In other words, these genetic and environmental differences aren't specific to alcohol, but affect many behaviors and interact with the tendency to drink in some way. One important study, again emerging out of a research group with strong ties to the Indiana Alcohol Research Center, explored a gene called GABRA2 that affects our brains, and interacts with a neurotransmitter called GABA. They found that there are two types of this gene; one type, which was previously shown to increase the risk for alcoholism in adults, also increased the risk for conduct disorder in adolescence, before heavy drinking sets in. Conduct disorder is a serious condition in which kids have repeated difficulties interacting with authority figures, and often get into arguments and fights with them as well as with their peers. They are also more likely to have problems with alcohol and drugs. Although previously scientists had focused on how GABRA2 might affect what alcohol itself does to the brain, this study showed that GABRA2 affects behavior even before drinking problems set in, and perhaps "sets the stage" for drinking problems to emerge. Kids who have trouble with authority figures intuitively would seem more likely to seek out alcohol, perhaps partly because they know that drinking "breaks the rules," and they may also seek out drinking *because* they know they're more likely to get into trouble when they're drunk.

These examples are interesting partly because although they are both genetic, heritable differences among us that alter the likelihood of becoming an alcoholic, two things stand out about them. First of all, they are not, by any means, deterministic. Inheriting a liver that makes you feel ill when you drink will reduce your chance of becoming an alcoholic by about two thirds – considerable, but there are still those with the altered liver metabolism who become alcoholics. Furthermore, the vast majority of us lack these altered livers, so they don't play a role in our drinking. GABRA2's effect is even more equivocal: when you inherit the "high drinking" variant of the gene, it might increase your risk of developing alcoholism by just 2 or 3 percent.

Second, even genetic differences are subject to environmental modulation. Just because a behavior is inherited doesn't mean that behavior is written at birth. One study, conducted by Danielle Dick and colleagues, sought out whether parents would make any difference in the trajectory of kids who were at risk for alcoholism and conduct disorder, because they'd inherited the high risk type of GABRA2 gene. When interviewing the parents, she found that those who were very involved with their kids – for example, they knew the names of their kids' best friends, and tended to know where they were – almost completely eliminated the influence of the GABRA2 gene on antisocial behavior in their kids. Parents who had little control over their kids' lives showed an effect of this gene that was even larger than normal. This is what behavioral geneticists call a "gene X environment interaction." Growing up in an environment with high parental involvement reduces the likelihood that a genetic tendency will yield long-term conduct problems.

When we seek to understand whether genes or environment are more important, our answer can't be that it is one or the other. Instead, we now understand that in alcoholism (as with many behaviors), genes, environment, and the interaction between the two all play important roles. The emerging field of genetics will not change any of these answers fundamentally, but will instead allow us to get a better handle on the exact ways in which genes and environment play their roles and, if we are lucky, how we might best intervene to reduce the risk that our teens will develop into alcoholics.

NEXT MONTH: Creating the "perfect alcoholic" in order to study the causes of alcoholism.

